Our study had a few strengths and limitations. The number of study participants was large enough for us to stratify the participants by estimated TB incidence rates for their countries of origin. One limitation was that the participation rate was small. Just ≈11% of foreign-born students at Keio University participated; therefore, the results obtained might not be representative of LTBI in all foreign-born students.

In conclusion, we found that estimated LTBI rates for foreign-born students in Japan from countries with high TB incidence rates were higher than those for students from countries with low TB incidence rates and for students from Japan. Based on our findings, we recommend that universities screen for LTBI using IGRAs in students from countries with high TB incidence rates (i.e., >100 cases/100,000 persons).

Acknowledgments

We are grateful to Satoshi Mitarai for his critical reading of our manuscript.

This research was supported by the Research Program on Emerging and Re-emerging Infectious Diseases from the Japan Agency for Medical Research and Development (JP17fk0108304) and Keio Gijuku Academic Development Funds. This research study was completed as part of our collaborative research with Oxford Immunotec, Ltd. (Abington, UK).

About the Author

Dr. Nishimura is a physician working as an assistant professor at Keio University. His primary research interest is mycobacterial diseases.

References

1. Kekkaku Yobo kai (Japan Anti-Tuberculosis Association). Kekkaku no toukei 2017 (Statistics of TB 2017) [in Japanese]. Tokyo: Kekkaku Yobo kai (Japan Anti-Tuberculosis Association); 2017.
2. The Japan Times. Tokyo reveals rare outbreak of tuberculosis, plays down ongoing risk [cited 2017 Nov 23]. https://www.japantimes.co.jp/news/2016/05/18/national/tokyo-reveals-rare-outbreak-of-tuberculosis-plays-down-ongoing-risk/
3. Public Health England. Non-UK born TB cases. In: Tuberculosis in England. 2015 Report (presenting data to end of 2014) version 1.1 [cited 2017 Nov 20]. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/564649/TB_annual_report_2015.pdf
4. Ogiwara T, Kimura T, Tokue Y, Watanabe R, Nara M, Obuchi T, et al. Tuberculosis screening using a T-cell interferon-γ release assay in Japanese medical students and non-Japanese international students. Tohoku J Exp Med. 2013;230:87–91. http://dx.doi.org/10.1620/tjem.230.87
5. World Health Organization. Tuberculosis country profiles [cited 2017 Nov 21]. http://who.int/tb/country/data/profiles/en/

Address for correspondence: Tomoyasu Nishimura, Health Center, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan; email: tnishimura@keio.jp

Effect of Inactivated Poliovirus Vaccine Campaigns, Pakistan, 2014–2017

Nicholas C. Grassly, Mufti Zubair Wadood, Rana M. Safdar, Abdirahman Sheikh Mahamud, Roland W. Sutter

Author affiliations: Imperial College London, London, United Kingdom (N.C. Grassly); World Health Organization, Geneva, Switzerland (M.Z. Wadood, R.W. Sutter); Ministry of National Health Services, Islamabad, Pakistan (R.M. Safdar); World Health Organization, Islamabad (A.S. Mahamud)

DOI: https://doi.org/10.3201/eid2411.180050

Pakistan began using inactivated poliovirus vaccine alongside oral vaccine in mass campaigns to accelerate eradication of wild-type poliovirus in 2014. Using case-based and environmental surveillance data for January 2014–October 2017, we found that these campaigns reduced wild-type poliovirus detection more than campaigns that used only oral vaccine.

Routine immunization with ≥1 dose of inactivated poliovirus vaccine (IPV) in all countries using oral poliovirus vaccine (OPV) was recommended by the World Health Organization (WHO) in November 2012, before the global withdrawal of the serotype 2 component from OPV (*1*). IPV has also been used since 2014 in mass campaigns to help interrupt wild poliovirus transmission and stop serotype 2 vaccine-derived poliovirus (VDPV2) outbreaks. The IPV supply was severely constrained during 2016–2017; only 2 manufacturers supply the United Nations Children's Fund, and their failure to produce the expected bulk product has meant that only about half the awarded quantities were supplied (*2*). As a result of these unplanned reductions in IPV supply, countries have delayed the introduction of IPV to routine immunization or faced stockouts, and mass campaigns with IPV in response to VDPV2 are no longer recommended by WHO (*3*). Nonetheless, where possible, IPV continues to be used in mass campaigns for outbreak response; for example, Pakistan, Afghanistan, Nigeria, and Syria all used IPV in mass campaigns in 2017.

Given that IPV supply constraints are likely to continue until at least the end of 2018, it is crucial that available IPV be optimally allocated between routine immunization and mass campaigns. We recently published estimates of the impact of OPV mass campaigns with and without the inclusion of IPV in Nigeria and Pakistan during January 2014–April 2016 (*4*). These estimates demonstrated a reduction in the incidence of poliomyelitis and detection of poliovirus in the environment after campaigns that used IPV in Nigeria but not in Pakistan, where statistical power was limited. We have now updated these estimates in Pakistan for January 2014–October 2017, thereby including a longer period of surveillance and additional campaigns during a period when wild-type 1 poliovirus has been circulating (online Technical Appendix, https://wwwnc.cdc.gov/EID/article/24/11/18-0050-Techapp1.pdf). We find evidence of an impact of campaigns that used IPV alongside OPV (bivalent, trivalent, or monovalent) on the incidence of poliomyelitis caused by wild-type poliovirus (incidence rate ratio [IRR] for 90 days after compared with before the campaign, IRR 0.62, 90% bootstrap CI 0.23–1.14), and a significant impact on the detection of this virus in environmental samples (prevalence ratio [PR] 0.63, 90% CI 0.47–0.81) (Figure; online Technical Appendix Table). The effect of campaigns using only bivalent OPV was less than the effect of campaigns that included IPV (IRR for poliomyelitis 0.79 [90% CI 0.64–0.98] and PR for environmental detection 0.92 [90% CI 0.83–1.00] for the 90 days after compared with before the campaign); this difference was statistically significant for detection of poliovirus in the environment (bootstrap p values 0.239 comparing the IRRs and 0.005 comparing the PRs for campaigns with and without IPV). We did not update estimates for Nigeria because only 2 campaigns using IPV occurred during April 2016–October 2017, in areas with very limited VDPV2 detection.

Several caveats relate to this analysis, reflecting its observational nature, reliance on routinely collected data, and lack of randomization. Campaigns that included IPV may have been implemented with different standards and, potentially, greater coverage, although data supporting this assertion have not been presented. It is often assumed that campaigns including IPV would have lower coverage because IPV must be administered by trained healthcare staff from fixed points rather than in house-to-house campaigns (*5*). Furthermore, these findings may not apply to more recent serotype-2 vaccine-derived poliovirus outbreaks, which have occurred in countries without recent use of a serotype-2–containing oral vaccine, thereby limiting boosting of mucosal immunity by IPV to older cohorts.

In conclusion, these updated estimates from Pakistan provide support for including IPV in mass campaigns with OPV to reduce poliovirus transmission, in agreement with results from Nigeria. Intradermal administration of a 1/5 fractional dose may allow dose sparing during these campaigns while maintaining comparable immunogenicity (*6*). These findings are informing discussions about the role of IPV in stopping the last remaining chains of wild-type 1 poliovirus transmission, responding to VDPV2 outbreaks, and protecting children who have not received vaccine containing serotype 2.

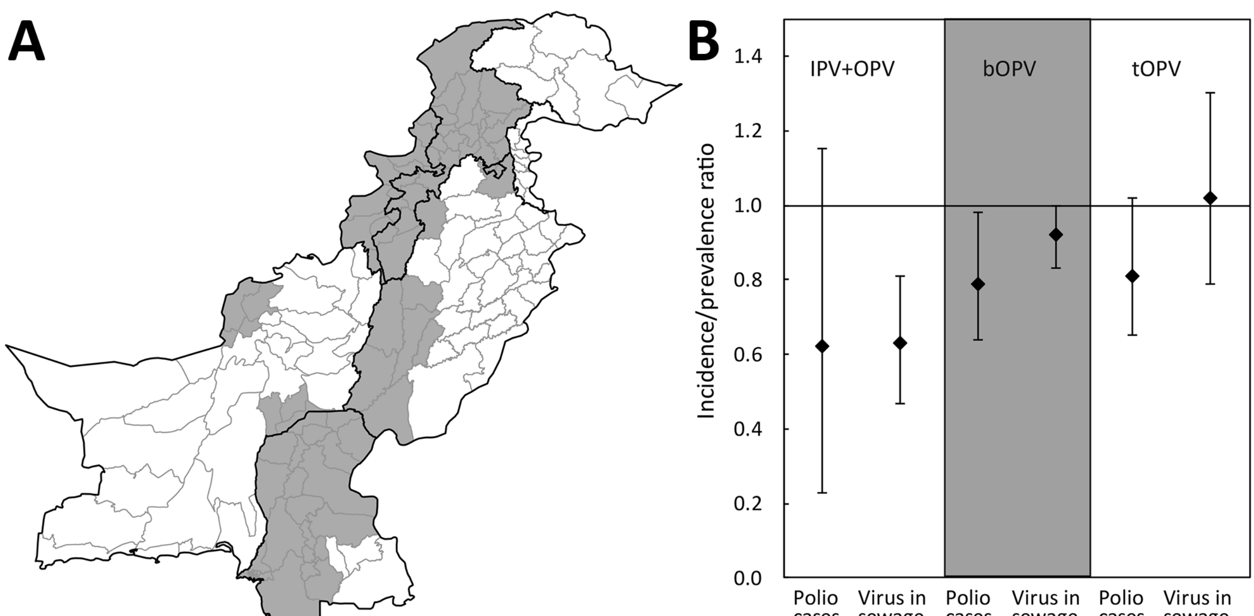

Figure. Location and impact of mass campaigns in Pakistan during January 2014–October 2017 that have included inactivated poliovirus vaccine (IPV) alongside oral vaccine. A) Gray shading indicates districts in Pakistan that conducted campaigns with IPV during January 2014–October 2017. B) The incidence rate ratio (IRR) for poliomyelitis and the prevalence ratio (PR) for poliovirus detection in environmental samples (sewage) during 90 days after compared with 90 days before mass vaccination campaigns with different vaccines. The mean estimates (diamonds) are shown with 90% bootstrap CIs (error bars). Detailed methods and results are given in the online Technical Appendix (https://wwwnc.cdc.gov/EID/article/24/11/18-0050-Techapp1.pdf). bOPV, bivalent oral poliovirus vaccine; IPV, inactivated poliovirus vaccine; tOPV, trivalent oral poliovirus vaccine.

Acknowledgments
We thank all those involved in the extensive efforts to implement clinical and environmental surveillance in Pakistan.

This work was supported by research grants from the World Health Organization (2013/363982) and the Bill and Melinda Gates Foundation (OPP1099374).

About the Author
Dr. Grassly is a professor of vaccine epidemiology in the department of infectious disease epidemiology at Imperial College London, London, UK. His primary research interests are the epidemiology of enteric viruses and immune response to infection and vaccination.

References
1. World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, November 2012—conclusions and recommendations. Wkly Epidemiol Rec. 2013;88:1–16.
2. Lewis I, Ottosen A, Rubin J, Blanc DC, Zipursky S, Wootton E. A supply and demand management perspective on the accelerated global introductions of inactivated poliovirus vaccine in a constrained supply market. J Infect Dis. 2017;216(suppl 1):S33–9. http://dx.doi.org/10.1093/infdis/jiw550
3. Global Polio Eradication Initiative. Standard operating procedures: responding to a poliovirus event or outbreak. V2.3 01; 2017 [cited 2017 May 7]. http://www.polioeradication.org
4. Shirreff G, Wadood MZ, Vaz RG, Sutter RW, Grassly NC. Estimated effect of inactivated poliovirus vaccine campaigns, Nigeria and Pakistan, January 2014–April 2016. Emerg Infect Dis. 2017;23:258–63. http://dx.doi.org/10.3201/eid2302.161210
5. Pervaiz A, Mbaeyi C, Baig MA, Burman A, Ahmed JA, Akter S, et al. Fractional-dose inactivated poliovirus vaccine campaign—Sindh Province, Pakistan, 2016. MMWR Morb Mortal Wkly Rep. 2017;66:1295–9. http://dx.doi.org/10.15585/mmwr.mm6647a4
6. Okayasu H, Sein C, Chang Blanc D, Gonzalez AR, Zehrung D, Jarrahian C, et al. Intradermal administration of fractional doses of inactivated poliovirus vaccine: a dose-sparing option for polio immunization. J Infect Dis. 2017;216(suppl 1):S161–7. http://dx.doi.org/10.1093/infdis/jix038

Address for correspondence: Nicholas C. Grassly, Imperial College London, Department of Infectious Disease Epidemiology, Norfolk Place, W2 1PG, UK; email: n.grassly@imperial.ac.uk

Enterovirus D68 Surveillance, St. Louis, Missouri, USA, 2016

Mythili Srinivasan, Angela Niesen, Gregory A. Storch

Author affiliations: Washington University, St. Louis, Missouri, USA (M. Srinivasan, G. Storch); St. Louis Children's Hospital, St. Louis (A. Niesen)

DOI: https://doi.org/10.3201/eid2411.180397

A fall 2016 outbreak of enterovirus D68 infection in St. Louis, Missouri, USA, had less effect than a fall 2014 outbreak on hospital census, intensive care unit census, and hospitalization for a diagnosis of respiratory illness. Without ongoing surveillance and specific testing, these cases might have been missed.

The largest known outbreak of enterovirus D68 (EV-D68) occurred in the United States in 2014 (*1*). Severe respiratory illnesses increased in fall of 2014, corresponding to a period when EV-D68 was present in the community, at St. Louis Children's Hospital (St. Louis, Missouri, USA) and elsewhere in the United States (*1,2*). Multiple reports suggested that the predominant virus was from clade B1, although some viruses from clades B2 were also detected (*3–5*). During 2015, there were few reports of EV-D68 circulating in the United States (*6*); however, in 2016, EV-D68 reappeared in multiple US locations (New York, Colorado); virus sequences suggested that the predominant virus was from clade B3 (*4*,*7*). We also documented EV-D68 activity in St. Louis in 2016. Sequencing of viruses from 2 patients tested in the St. Louis Children's Hospital virology laboratory revealed clade B3 with 99% identity to the clade B3 virus from New York (*8*). Our goal with this study was to determine if the 2016 outbreak had caused an increase in hospital census or increase in patients admitted with respiratory diagnosis, as was seen during the 2014 outbreak.

During August 7, 2016, through December 16, 2016, we used a previously described EV-D68–specific PCR to test 5%–10% of enterovirus/rhinovirus–positive samples submitted each week to the St. Louis Children's Hospital diagnostic virology laboratory. The samples had been obtained from patients seen at the hospital's emergency department or clinics or admitted to the inpatient units and had been routinely tested by a FilmArray Respiratory Panel (BioFire, Salt Lake City, UT, USA) (*9*). Samples were selected by laboratory staff without regard to patient characteristics and were deidentified before EV-D68 testing. We obtained inpatient and intensive care unit (ICU) census data for all patients (not limited to those with a

Article DOI: https://doi.org/10.3201/eid2411.180050

Effect of Inactivated Poliovirus Vaccine Campaigns, Pakistan, 2014–2017

Technical Appendix

Data

Pakistan implements acute flaccid paralysis and environmental surveillance for polioviruses (*1*). We extracted these surveillance data together with the vaccination campaign calendar for the period January 2014–October 2017 from the Polio Information System (PolIS) on December 16, 2017. Campaigns with inactivated poliovirus vaccine (IPV) and oral poliovirus vaccine (OPV) recorded as occurring within 14 days were considered the same campaign in this analysis (i.e., IPV+OPV). Administrative boundaries for the map in the Figure in the print article were provided by the World Health Organization. The publication of this map does not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Estimates of the number of children 0–14 years of age living in each district were obtained as described previously (*2*).

Statistical Analysis

We calculated the incidence of poliomyelitis associated with serotype-1 wild poliovirus and the prevalence of this virus in environmental samples in the 90 days before and after mass campaigns using different vaccine types in each district of Pakistan. We used mixed-effects Poisson or binomial regression to estimate the incidence rate ratio (IRR) or prevalence ratio (PR) for poliomyelitis incidence or environmental detection of poliovirus after a campaign compared with before the campaign. Full details of the methods are given by Shirreff et al. (*2*). When 2 or more campaigns took place in a district within 180 days such that the observation periods overlapped, we censored the data to avoid the inclusion of nonindependent (repeated) data in the analysis. We randomly selected the order in which districts and campaigns were included in the analysis, prioritizing campaigns that included IPV. This meant that some campaigns were associated with <180 days observation or were not included in the database. Here we report a range for the number of campaigns, incidence of poliomyelitis, and prevalence in environmental samples based on 1,000 repetitions of this process. The IRR and PR were estimated along with their 90% confidence intervals based on the mean and the 5th and 95th percentiles for their values for 1,000 bootstrap replicates of the data, sampling with replacement (i.e., without censoring) to describe the sampling distribution of these statistics following standard procedures (*3*).

References

1. Elhamidi Y, Mahamud A, Safdar M, Al Tamimi W, Jorba J, Mbaeyi C, et al. Progress toward poliomyelitis eradication—Pakistan, January 2016–September 2017. MMWR Morb Mortal Wkly Rep. 2017;66:1276–80. PubMed http://dx.doi.org/10.15585/mmwr.mm6646a4

2. Shirreff G, Wadood MZ, Vaz RG, Sutter RW, Grassly NC. Estimated effect of inactivated poliovirus vaccine campaigns, Nigeria and Pakistan, January 2014–April 2016. Emerg Infect Dis. 2017;23:258–63. PubMed http://dx.doi.org/10.3201/eid2302.161210

3. Efron B, Tibshirani R. Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. Stat Sci. 1986;1:54–75. http://dx.doi.org/10.1214/ss/1177013815

Technical Appendix Table. Incidence of poliomyelitis associated with wild-type 1 poliovirus and prevalence of this virus in environmental samples in Pakistan in the 90-day period before and after campaigns with different vaccine types.*

Vaccine	State	District campaigns included in analysis (n)†	Range of incidence of poliomyelitis (n cases/100,000 child-years)‡ Before	After	IRR (90% bootstrap CI)	Prevalence in environmental samples, range (%) Before	After	PR (90% bootstrap CI)
IPV+ OPV	All	166	(17–28)/ (162–165)	(7–17)/ (158–160)	0.62 (0.23–1.15)	25 (24–26)	15 (14–16)	0.63 (0.47–0.81)
	Balochistan	14	(10–15)/ (9.53–10.8)	(2,4)/ (9.53–10.8)		45 (42–48)	25 (22–28)	
	FATA	17	(1,2)/ (6.25,6.25)	(0,6)/ (6.25,6.25)		NA	NA	
	Gilgit Baltistan	0	0/0	0/0		NA	NA	
	Islamabad	2	0/ (1.65–1.65)	0/ (0.33–0.33)		0 (0–0)	NA	
	Khyber Pakhtunkhwa	57	(5–10)/ (59.6–59.6)	(5,7)/ (59.6–59.6)		25 (22–25)	8 (8–8)	
	Punjab	9	0/ (26.1–26.1)	0/ (23.1–23.1)		14 (14–14)	21 (21–21)	
	Sindh	67	(1–2)/ (58.8–60.3)	0/ (58.8–60.3)		16 (15–16)	11 (11–12)	
bOPV	All	1330–1392	(102–192)/ (997–1081)	(77–165)/ (962–1042)	0.79 (0.64–0.98)	20 (17–24)	20 (15–23)	0.92 (0.83–1.00)
	Balochistan	241–265	(5–14)/ (39.3–49.2)	(4–13)/ (38.3–47.4)		31 (21–41)	27 (16–38)	
	FATA	107–124	(31–103)/ (21.6–28.5)	(35–91)/ (20.7–26.8)		NA	NA	
	Gilgit Baltistan	53–63	(0–1)/ (4.76–5.98)	(0–1)/ (4.87–6.06)		NA	NA	
	Islamabad	12–18	0/ (7.04–11.8)	0/ (7.25–12.9)		22 (6–38)	19 (5–33)	
	Khyber Pakhtunkhwa	172–195	(20–53)/ (110–134)	(12–43)/ (99.8–122)		15 (9–23)	19 (8–30)	
	Punjab	296–324	(2,6)/ (561–630)	(0–3)/ (554–629)		11 (8–15)	9 (5–13)	
	Sindh	324–349	(19–33)/ (207–237)	(13–28)/ (185–212)		31 (24–38)	33 (25–41)	
tOPV	All	81–105	(3–62)/ (45.5–90.1)	(0–30)/ (39.5–72.6)	0.81 (0.65–1.02)	7 (6–20)	20 (8–50)	1.02 (0.79–1.30)
	Balochistan	22–27	0/ (1.81–4.99)	(0–2)/ (1.81–3.96)		NA	NA	
	FATA	0–8	(0–55)/ (0–1.23)	(0–23)/ (0–1.37)		NA	NA	
	Gilgit Baltistan	7–7	0/ (0.15–0.86)	0/ (0.25–0.83)		NA	NA	
	Islamabad	0–2	0/ (0–1.65)	0/ (0–1.18)		0 (0–0)	0 (0–0)	
	Khyber Pakhtunkhwa	6–16	(0–5)/ (3.70–15.84)	(0–5)/ (2.03–9.01)		NA	NA	
	Punjab	21–31	(0–2)/ (22.71–62.13)	0/ (22.3–54.2)		0 (0–0)	0 (0–0)	
	Sindh	4–16	0/ (2.03–10.46)	(0–1)/ (1.48–11.2)		33 (17–33)	100 (67–100)	

*IRR = incidence rate ratio; NA, not available; PR = prevalence ratio.
†Counts campaigns in each district separately (e.g., a campaign covering 5 districts would be counted as 5 district campaigns). When calculating the number of campaigns, incidence, and prevalence, we included only those providing independent data after-censoring observations with overlapping tin periods (see Methods in the print article and this Technical Appendix). The order of censoring can affect this number, so we randomly added campaigns to the analysis database, prioritizing those that included IPV. We show the range from 1,000 replicates of this random selection procedure. The number of campaigns with IPV did not vary because these were prioritized in the censoring process, so only a single number is shown.
‡Child-years are based on estimates of children aged 0–14 y, corresponding to the age range for AFP surveillance. The range in the number of cases and child-years included in the analysis for each random sample of the data are shown in the numerator and denominator, respectively.